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CHEMICAL NATURE AND MODE OF FORMATION OF PEPSIN, TRYPSIN AND BACTERIOPHAGE[1]

By Dr. JOHN H. NORTHROP

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THE field of enzymes has always been a sort of no-men's land between the fields of chemistry and biology. In the early days of science reactions occurring in, or caused by, living organisms were grouped together as fermentations and were supposed to be qualitatively different from the reactions of inorganic material. In the course of the nineteenth century the work of Payen and Persoz, Schwann, Kühne and Buchner and many others showed that most of these reactions were caused by the presence of unknown substances formed by the living cells, but which were not living. These substances were called "enzymes" by Kühne. Berzelius early pointed out that these reactions were very similar to the catalytic reactions of inorganic chemistry, and the work of Tamman, Arrhenius, Henri, Michaelis, Nelson, Euler, Willstätter, Warburg and other chemists has shown that this view was correct. It is only recently, however, that enzymes have been accepted as a part of chemistry and it is very gratifying that research on enzymes should be selected for a chemical award.

The chemical nature of the enzymes themselves remained quite unknown until a few years ago. In the last eleven years a number of enzymes have been isolated and crystallized and have been found to be proteins. The hydrolytic enzymes, urease (Sumner), pepsin[2] (Northrop), trypsin,[2] chymo-trypsin[2] (Kunitz and Northrop), carboxypeptidase[2] (Anson), amylase

[1] Lecture delivered on the occasion of the presentation of the Charles Frederick Chandler Medal of Columbia University on October 27, 1937. The lecture was illustrated by lantern slides.

[2] Photographs of these preparations are reproduced in Harvey Lectures, 1934–35, p. 229.

(Caldwell, Booker and Sherman), a proteolytic enzyme from Ficis (Walti) and from papain (Balls, Lineweaver and Thompson) appear to be simple proteins, since no evidence of a prosthetic group (a group other than an amino acid) has been found, while Warburg's respiratory ferment, which is an oxidative catalyst, is a conjugated protein and contains a prosthetic group. Sumner and Dounee have recently crystallized catalase, and this enzyme also contains a prosthetic group.

It appears, therefore, that the characteristic chemical reactions occurring in living cells are caused by the presence of minute amounts of certain peculiar proteins, so that the nature and mode of action of enzymes is now fairly well established.

In the meantime, however, a new controversy over the nature of "viruses" has arisen, quite similar to the early controversy over the nature of enzyme reactions. Iwanowski and Beijerinck described the first of these active agents at about the time of Buchner's experiments. A large number of such filterable viruses were soon described, among them the bacteriophage of Twort and d'Herelle which possesses the remarkable property of dissolving bacteria. These filterable viruses increase in quantity in the presence of living cells and for this reason have been considered by many workers to be themselves living organisms.

The biological properties of bacteriophage have been determined by d'Herelle, who has shown that they are closely analogous to those of living cells.

Bordet, on the other hand, has shown that the facts may be more simply explained by assuming the autocatalytic production of phage from a normal cell constituent. It has been found recently that pepsin and trypsin, under the proper conditions, also increase, and there are, of course, many other known autocatalytic reactions so that the property of increasing in quantity or growth can not be considered a definite criterion for the presence of living cells. Stanley has isolated and crystallized a protein which appears to be the active agent of the tobacco mosaic, and the writer has obtained a nucleo protein which appears to be the bacteriophage. Some filterable viruses, therefore, are probably enzymes which possess the property of forming themselves under proper conditions.

Chemical Nature of the Enzymes

The isolation of enzymes in the form of crystalline proteins shows that they are essentially protein in character. Since these proteins exhibit peculiar properties they must have peculiar chemical structure, and since the chemical properties of molecules are not additive the entire structure of the molecule must be known before the properties of the molecule are completely understood. It is usually true, however, that certain chemical properties depend markedly on certain groups or atoms in the molecule and to a much less extent upon other groups or atoms. These groups, which markedly influence the activity, are frequently referred to as "active groups," but it must be realized that the term is relative and that theoretically a change in any part of the molecular structure would be expected to influence the properties of the molecule. In the case of the yellow respiratory ferment Warburg has shown that the activity depends on the presence of a characteristic prosthetic group and has determined the general nature of the group so that the most important part of the structural chemistry of this enzyme is now known.

The proteolytic enzymes may also have prosthetic groups, but there is, as yet, no evidence for their presence so that the activity appears to depend on some peculiar arrangement of the amino acids, as is probably the case in insulin. Attempts to isolate fragments of the molecule possessing some peculiar structure have failed, since the activity is lost as soon as the molecule is ruptured and there is no means, at present, once the enzymatic activity is lost, of recognizing the fragments which possess the "active group."

It has been possible, however, to prepare several proteins closely related to the active enzymes, but which are themselves inactive, and a study of the difference between these inactive proteins and the active enzymes has thrown some light on the structure responsible for the activity as well as upon the method of formation of the active enzyme in the animal body.

The results in general indicate that comparatively slight changes in an inactive protein may result in the formation of an active enzyme and that under certain conditions this reaction is autocatalytic, *i.e.*, some enzymes possess the power to form themselves from inert proteins.

Isolation and Crystallization of Pepsin, Trypsin, Chymo-Trypsin and Their Precursors

Unfortunately experience has shown that no one method can be relied upon to lead to the isolation and crystallization of enzymes. The most that can be said is that they are best handled by the technique of protein chemistry and that large quantities must be used so that weighable solid precipitates are available and not simply dilute solutions.

In the work reported here this has been the guiding principle, and several grams or, better several hundred grams, of each step in the process of purification have been at hand before proceeding to the next step.

Pepsin

Pepsin was isolated and crystallized from commercial pepsin preparations by precipitation with mag-

nesium sulfate in dilute acid. It has also been obtained from bovine gastric juice. Active pepsin exists only in the gastric juice and is present in the gastric mucosa as an inert protein, pepsinogen. Pepsinogen has also been obtained in crystalline form by extraction from the mucosa in slightly alkaline solution and fractionation by means of ammonium sulfate.

Pancreatic Enzymes

Digestion of proteins in the small intestine is caused by the pancreatic juice, and it was thought at first that this juice contained only one proteolytic enzyme called by Kühne "trypsin." It is now known, however, from the work of Willstätter, Waldschmidt-Leitz and others that pancreatic juice contains a series of proteolytic enzymes, erepsin, aminopolypeptidase, carboxypolypeptidase, protaminease, chymo-trypsin and probably others. Like pepsin, the enzymes in the pancreatic juice became active only after secretion and are present in the gland itself in the form of inactive precursors. Trypsin was originally isolated and crystallized from activated pancreatic extract by repeated fractionation with ammonium sulfate. The procedure was difficult, however, and a much more efficient method was worked out by which the inactive precursor of trypsin (trypsinogen)[2] was isolated from inactive acid extracts of fresh pancreas. The inactive precursor of chymo-trypsin was also isolated from such extracts, as well as a substance which powerfully inhibits trypsin activity. Anson isolated and crystallized carboxypeptidase from activated pancreatic extract and was able to show that this enzyme also exists in fresh pancreas in an inactive form. Conditions for the transformation of the inactive precursors to the active enzymes have beeen worked out and the active enzymes themselves crystallized.

Purification of Bacteriophage

A nucleo protein has been isolated from lysed staphylococci culture which has the properties of bacteriophage, *i.e.*, it increases when inoculated into a growing culture of staphylococci and eventually causes complete dissolution of the bacteria. The protein is practically homogeneous in the ultra-centrifuge and has a sedimentation constant of about 650×10^{-13} cm dym^{-1}, sec^{-1} corresponding to a molecular weight of about 200 million. The minimum quantity of the nucleo protein which can be detected is about 5×10^{-16} gm. If this quantity is assumed to be one molecule then the gram molecular weight of the substance is about 300 million gm. This is about the same order of magnitude as the molecular weight by the sedimentation velocity method. Diffusion measurements in concentrated solution show that the protein and the active agent diffuse at the same rate and give a value for the molecular volume which agrees approximately with that found by the centrifuge method. In extremely dilute solution the phage diffuses more rapidly, indicating that the phage particle may dissociate into smaller units as do the hemocyanins. Similar results have been previously reported by Bronfenbrenner.

Relation of Activity to the Protein

The preparations obtained in this way (with the exception of bacteriophage) are all crystalline proteins and may be recrystallized many times without change in properties. The most rigorous test of purity of a protein is solubility measurements, which take the place of the ordinary melting point. Such solubility determinations have been carried out on pepsin, pepsinogen, trypsin, chymo-trypsin and chymo-trypsinogen. The results show that the solubility is independent of the quantity of solid phase present and hence that the solid phase consists of only one component. This furnishes strong evidence that the activity is really a property of the protein molecule. The solubility of bacteriophage is constant in the presence of a large excess of solid but varies somewhat with smaller quantities of solid. The preparation, therefore, still contains two or more components one of which is probably an inactivated form of the other.

It may be shown, in addition, that loss in activity is accompanied by changes in the chemical properties of the protein. Thus, when phage or the enzymes are heated the activity is lost and at the same time denatured protein is formed. In the case of trypsin and chymo-trypsin the reaction is rapidly and completely reversible so that these enzymes exist in equilibrium with an inactive, denatured form. This equilibrium is accurately expressed by van't Hoff's equation connecting the heat of reaction and the effect of temperature on the equilibrium constant and gives a value for the latter of 67,000 calories per mol. In the case of pepsin the denatured pepsin may also be reconverted to native active pepsin. The equilibrium between native and denatured trypsin is also affected by the pH of the solution, and this accounts in part for the effect of the pH on the activity of the enzyme.

The relation between protein and activity may be further tested by digesting the protein with another enzyme. If trypsin or chymo-trypsin is hydrolyzed by pepsin there is a loss in activity corresponding to the destruction of the protein. Digestion of phage with chymo-trypsin leads to the formation of insoluble inactive protein. If the rate of diffusion of the protein and the activity is determined it is found that the diffusion proceeds at the same rate when followed by either method. The active molecule and the protein molecule therefore diffuse at the same rate.

Gates showed that the efficiency of various wave-

lengths of ultra-violet light on the inactivation of pepsin is the same as that for the relative absorption at various wave-lengths by pepsin solutions. The result indicates that each quantum absorbed by a protein molecule inactivates the molecule. Similar results were obtained with bacteriophage.

These experiments indicate strongly that the activity is a property of the protein molecule itself but unfortunately furnish no information as to the chemical structure in the molecule responsible for its activity. Owing to the extreme complexity of the protein molecule it is impossible, at present, to determine the structural configuration of the whole molecule, but some information in this connection has been obtained by studying the known changes in the molecule which affect the activity. The most definite of these reactions is the formation of acetyl derivatives of pepsin. Two crystalline[2] acetyl derivatives have been obtained by the action of ketene in aqueous solution at pH 5.0–6.0. The first compound contains 3 or 4 acetyl groups attached to the primary amino groups. It has the same activity as the original pepsin. A second derivative containing 7 acetyl groups has also been obtained. It has 60 per cent. of the activity of the original pepsin. On standing in acid this compound loses half of its acetyl groups and at the same time regains its original activity. Those acetyl groups, which decrease the activity and are removed by standing in acid, are attached to the hydroxyl group of tyrosine. Substitution of iodine for the hydrolyl groups of tyrosine also decreased the activity. These results show that the free amino groups of pepsin are not necessary for the activity, but that the phenolic groups of tyrosine are essential to the enzymatic activity.

Formation of Enzymes from Their Inactive Precursors

Further knowledge concerning the chemical structure responsible for the enzymatic activity of the molecule has been obtained by a study of the formation of the active enzymes from their inactive precursors.

Chymo-trypsin from chymo-trypsinogen[2]*:* Heidenhain and Kühne showed that freshly secreted pancreatic juice was inactive but becomes active when mixed with the secretion of the small intestine. It was assumed, therefore, that the enzymes were present in the pancreas in an inactive form. The formation of the active enzymes from inactive pancreatic juice or from inactive extracts of pancreas has been extensively studied, but the literature is surprisingly confused and contradictory. The course of the reaction has been described as catalytic, stoichiometric and autocatalytic. These contradictory results were obtained with crude preparations and under the conditions of the various experiments are probably all correct. During the course of the work on the isolation of the inactive form (chymo-trypsinogen) of chymo-trypsin and of the inactive form (trypsinogen) of trypsin we also obtained a number of apparently inexplicable, contradictory results. These varying results were eventually found to be caused by the presence in amorphous chymo-trypsinogen preparations of more or less trypsinogen and of a substance[2] which inhibits trypsin. Small amounts of these impurities influence the activation very markedly and until the protein was crystallized the activation experiments could not be repeated with certainty. When the chymo-trypsinogen has been recrystallized several times it is freed from inhibitor and trypsinogen, and its activation by trypsin becomes a perfectly definite and reproducible catalytic reaction. The rate is proportional to the trypsin concentration and also to the chymo-trypsinogen concentration. The rate of activation by trypsin is affected by the acidity of the solution in the same way as is the rate of digestion of other proteins by trypsin so that the reaction appears to be analogous to ordinary protein hydrolysis. There is one striking difference, however, in that, so far as we have been able to determine, nothing is split from the chymo-trypsinogen molecule, although there is an increase of 5 amino groups per mol. The formation of the active form from the inactive form of chymo-trypsin, therefore, may be due to the opening of a peptide ring. The isoelectric point is shifted from about pH 5.0 to about pH 5.4 and there is a slight decrease in optical rotation, but no other chemical differences have been detected so far. The elementary analysis, the tyrosine plus tryptophane content, the diffusion coefficient and molecular weight of the enzyme and of its precursor are the same within the experimental error. The x-ray defraction patterns of the two substances, according to Wyckoff, are quite different and show no more resemblance than would be expected between any two different proteins. Ten Broeck has shown that the two proteins may be distinguished by means of the anaphylactic test.

In addition to the activation by trypsin, very slow activation occurs in slightly acid solution. The activation is not accelerated by pepsin, chymo-trypsin itself, enterokinase or trypsinogen.

Trypsin from trypsinogen: As in the case of chymo-trypsinogen the activation of trypsinogen changes markedly after crystallization. Amorphous preparations are stable in solution and can only be activated by the addition of kinase (an extract of the small intestine), by large quantities of trypsin or by the addition of concentrated magnesium or ammonium sulfate solutions. After crystallization, however, the protein becomes transformed very rapidly into the active enzyme as soon as it is dissolved in neutral solution. This change in behavior is due to the fact

that amorphous preparations contain traces of a substance which inhibits trypsin and so prevents the autocatalytic reaction. As soon as this inhibitor is removed by crystallization the most minute trace of trypsin starts the activation reaction, which then proceeds autocatalytically. This reaction agrees quantitatively with the theory for a simple autocatalytic reaction. The velocity is affected by acidity and temperature in the same way as is the activation of chymotrypsinogen or hydrolysis of other proteins by trypsin. At pH 5.0 and 8° C. the value of the constant is 14.6, *i.e.*, with unit concentration of trypsinogen the active trypsin would increase 14 times per hour. This reaction evidently has a formal resemblance to bacteria growth curves. The addition of trypsin inhibitor to such solutions causes the production of a long lag period, and the curves obtained under these conditions are very similar to the usual bacterial growth curves. As in the case of chymo-trypsin there is no evidence for the splitting off of any part of the molecule during this activation reaction nor is there any marked change in chemical composition so that the change from the inactive protein to the enzyme is probably due to some internal rearrangement in the structure of the molecule. However, the work on this question is still in the preliminary stage. The autocatalytic nature of this reaction was correctly described by Vernon but subsequently denied by Bayliss and Starling and others.

Kunitz has recently found that trypsin is formed by trypsinogen at pH 5.0 by a proteolytic enzyme secreted by a mold (Penicillium). Trypsin is inactive at this pH, so that the activation curve is no longer autocatalytic but simply logarithmic as is the activation of chymo-trypsin. Trypsin obtained in this way is identical with that formed by autocatalytic activation. The mold enzyme, therefore, must attack the molecule at the same place as does trypsin.

Pepsin from pepsinogen: Langley showed that pepsin existed in gastric mucosa in a form which differed from the active enzyme in that it was much more resistant to alkali. Herriott has recently succeeded in isolating and crystallizing this substance. It has no proteolytic activity, but in slightly acid solution becomes converted into active pepsin. The reaction at pH 4.65 is autocatalytic and hence is caused by pepsin itself. About 15 per cent. of the nitrogen is split off during this reaction. So far as is known, pepsin attacks only peptide linkages so that there is reason to believe that the rupture of one or more peptide links in the precursor leads to the formation of the active enzyme. If swine pepsinogen is activated by chicken pepsin, swine pepsin is formed. The structure responsible for the species specificity of the enzyme therefore is present in the precursor.

Kinetics of the formation of bacteriophage: Bacteriophage, in common with the other viruses, possesses the property of increasing in the presence of living cells. In the case of bacteriophage the phenomenon may be quantitatively described under certain conditions by assuming that the percentage increase in the concentration of bacteriophage is proportional to the percentage increase in the number of bacteria per cc and that when the ratio of phage to bacteria passes a certain critical value the bacteria dissolve.

Under the usual conditions no increase in phage occurs without increase in bacteria, and it was thought at first that the multiplication of bacteria was a necessary condition for the increase of phage. Krueger has recently shown that the phage does increase under certain conditions without a corresponding increase in the number of bacteria. The formation of phage is, therefore, formally at least, analogous to the autocatalytic formation of trypsin from trypsinogen. The analogy extends even to the presence of a phage inhibitor in bacterial suspensions (Burnett, Levine) corresponding to the trypsin inhibitor in crude trypsinogen solutions. This inhibitor is responsible for the difficulty encountered in producing autocatalytic activation of trypsin in crude trypsinogen solutions. Krueger has recently shown that this phage inhibitor also interferes in the production of phage in cell free extracts and that when the inhibitor is removed a small increase in phage may be noted in such cell free extracts.

The assumption that phage produces itself autocatalytically from a precursor present in normal cells appears to fit the facts at present. This assumption is far simpler than the complicated series of assumptions involved in the idea that the phage is a living organism and avoids the difficulty of accounting for the necessary energy, if it is assumed that the phage synthesizes itself from simpler compounds.

OBITUARY

EDWARD LEAMINGTON NICHOLS

EDWARD LEAMINGTON NICHOLS was born in Leamington, England, on September 14, 1854, of American parents. After his graduation from Cornell in 1875 he studied in Leipzig, Berlin and Göttingen; and from the latter university received the degree of doctor of philosophy in 1879. During the year 1879–80 he held a fellowship in the Johns Hopkins University and in the following year was one of the assistants of Edison in his famous Menlo Park Laboratory. In 1881 he became professor of physics and chemistry at Central University in Kentucky; in 1883, professor of

physics and astronomy in the University of Kansas. In 1887 he returned to Cornell, where he remained as head of the department of physics until his retirement from active teaching in 1919. He died on November 10, 1937.

Nichols's activity as an investigator began when he was still a student and extended to within only a few years of the time of his death. Neither lack of facilities nor pressure of other work could lessen his interest or greatly reduce his activity. During his first year as a college teacher, many miles from a railroad and with no provision for apparatus or laboratory equipment, he carried on a difficult and dangerous experimental investigation on the undercooling of vapors. When for a period of two years he served not only as head of the department of physics at Cornell but also as dean of the College of Arts and Sciences, he still continued his experimental work on luminescence. Nichols was a firm believer in the value of scientific research to humanity. But he also greatly enjoyed his experimental work for its own sake. One might almost say that his belief in the value of science was as much the justification as the cause of his scientific activity. In my long association with him I was again and again impressed by the vigorous and almost joyous way in which he met and overcame experimental difficulties and by his enthusiastic welcome of new and unexpected results. His attitude was that of a young athlete engaged in a game which called for all his energy and skill, and which for that very reason he thoroughly enjoyed. No one could be associated with him long either as student or colleague without acquiring in some degree this same attitude toward scientific work.

In his work as an investigator he contributed to almost every branch of the physics of his day and was a pioneer in several important fields, such as illumination, physiological optics and luminescence. In recognition of this pioneer work he was awarded the Ives Medal of the Optical Society, the Elliott Cresson Medal of the Franklin Institute and the Rumford Medal of the American Academy, and was made an honorary member of the American Optical Society and of the Illuminating Engineering Society. In the case of the latter society Nichols and Edison were for many years the only recipients of this honor.

Nichols's enthusiasm for his subject and his friendly and sympathetic interest in the problems and difficulties of his students made him a most inspiring teacher. Not long after he became head of his department in 1887, it was my good fortune to spend a year as a graduate student under his guidance and I can well understand the reason for the respect and affection which all his students since have felt for him. Later as a junior member of the department I saw how he was able to inspire the whole staff with his own enthusiasm; encouraging us to develop our own ideas and methods, while protecting us by friendly comments from the serious blunders of inexperience, and giving us finally far more than proper credit for the results accomplished. Later still, for nearly twenty years, we did our experimental work together and published the results in joint articles. During these years Nichols's attitude toward our experimental work was a continual revelation to me of the scientific spirit at its best. The same spirit was shown in his treatment of matters outside the field of science, and his wise and altogether unprejudiced approach to the general educational problems of the university made him a most valuable member of the faculty.

In these days of rapid progress and widespread interest in all branches of science it is hard to realize how insignificant was the contribution of this country to the physical sciences sixty years ago. In only a few universities was scientific investigation actually under way, or even regarded as a proper function of the college teacher. Industrial research laboratories were not even mentioned as a possibility. Nichols contributed more than any other physicist of his generation to change this situation, and he was almost the last remaining member of that small group of men who kept physics alive in this country during the last two decades of the last century and prepared the way for the remarkable progress of the last twenty years. His enthusiasm and untiring activity as a scientific investigator served as an inspiration to others. As president of the Physical Society, of Sigma Xi and of the American Association for the Advancement of Science, he kept continually before the public the importance of scientific work. He was one of the most active of the small group who organized the American Physical Society in 1899. The *Physical Review*, founded by Nichols in 1893 and conducted for the first twenty years under his editorship, was the first journal of physics in this country and was an important factor in stimulating scientific activity.

Almost equally important was the indirect influence which Nichols exerted through the students who had received their inspiration from him and who later entered the field of college teaching or industrial physics. At the time of his retirement the heads of the departments of physics in thirty-five colleges, fifteen of them state universities, were men who had received their physics training from him. Add to this list the large number of his students who held important posts in government and industrial laboratories, or who were college teachers but not department heads, and we get some idea of the extent of his indirect influence on American physics.

For one who was as successful as he in a special field Nichols's interests and information extended over a surprisingly wide range. He was by no means a

narrow specialist. Undoubtedly this breadth of knowledge and interest was an important factor in making him so successful as a teacher. He was an enthusiastic traveler and although his sabbatical leave was usually spent in Europe had visited at some time each of the six continents. He was a most delightful companion on a journey, whether in fair weather or foul. A sincere and active church member, Nichols saw no conflict between science and religion, but merely two different aspects of that search for truth to which his life had been devoted. He will be held in affectionate remembrance by all who knew him, but especially by those of us who as his students and associates received encouragement and inspiration from his life and work.

ERNEST MERRITT

RECENT DEATHS

PROFESSOR T. NELSON DALE, formerly professor of geology at Vassar College and Williams College and for twenty-eight years—1892–1920—geologist of the U. S. Geological Survey, died on November 16. He would have reached the age of ninety-two years on November 25.

DR. CHARLES B. LINDSLEY, professor of mathematics at the University School, Cincinnati, Ohio, died on November 17 at the age of fifty-six years.

SCIENTIFIC EVENTS

ERADICATION OF THE DUTCH ELM DISEASE

FEDERAL forces made gains during the past summer in the fight on Dutch elm disease. The number of diseased trees found this year dropped twenty-five per cent. below last year in the territory where the infection is known to be of a serious epidemic character—an area extending fifty miles radially from New York City into Connecticut, New York State and New Jersey.

The disease has spread to no new territory this year, nor has it recurred in Baltimore, Brunswick and Cumberland, Md., Norfolk, Va., or Cleveland and Cincinnati, Ohio, where seventy-eight infected trees had been found in the past. Apparently they were discovered and removed in time to keep them from becoming sources of new infection. The only new centers of infection brought to light this season were one diseased elm at Athens, Ohio, and five diseased elms at Wileys Ford, W. Va. These trees have been destroyed. New infections along the boundaries of the major zone were limited to single trees in Alexandria Township, Hunterdon County, N. J.; Cornwall Township, Orange County, N. Y., and the town of Redding, Fairfield County, Conn.

There were 3,100 workers in the field from May 29 to October 1, and three examinations were made in the major area of infection and two in the 10-mile wide protective zone around it. Investigations in Indianapolis, Ind., where the disease has been present since 1934, showed an increase this year. Laboratory cultures of twig specimens from suspected trees proved the presence of the infection in 31 trees. All have been removed. As the campaign advances, it is necessary to look more closely for evidences of the disease and samples of all elms showing any symptoms of abnormality were collected. Twig samples from more than 75,000 elms with yellowed or wilting leaves and signs of brown streaks beneath the bark were sent to the laboratory for the culturing that proves the presence or absence of the disease.

An autogiro observer investigated 11,000 miles of railroad rights of way, over which the imported logs that brought the disease to this country traveled inland to be made into veneer for the cabinet makers. A follow-up ground crew visited points marked on his map. Three other autogiros were used to carry investigators over inaccessible areas in and around the major zone.

Winter activities will center on the removal of dead and devitalized elms, not necessarily infected with Dutch elm disease, but which furnish breeding places for the elm bark beetles that spread the fungus from infected to healthy trees. All elms will be removed from some areas of heavy infection and from certain swamp or mountain areas where summer work is particularly difficult and dangerous. This will make it impossible for the fungus to persist and for insect carriers to survive in areas where all diseased trees have been destroyed. In summarizing the season's activities for 1937, Lee A. Strong, chief of the Bureau of Entomology and Plant Quarantine, commended the aid given by WPA labor.

THE FINNEY-HOWELL RESEARCH FOUNDATION

AT the death of the late Dr. George Walker, of Baltimore, his will provided for the formation of a corporation to be known as the Finney-Howell Research Foundation, the purpose of which was to be the support of "research work into the cause or causes and the treatment of cancer." The will directed that the surplus income from the assets of the foundation together with the principal sum should be expended within a period of ten years to support a number of fellowships in cancer research, each with an annual stipend of two thousand dollars, "in such universities, laboratories or other institutions, wher-

ever situated, as may be approved by the Board of Directors."

In accordance with Dr. Walker's wishes the Finney-Howell Research Foundation has been duly incorporated under the laws of the State of Maryland, and the board of directors announce that they are prepared to award fellowships under the following regulations:

1. Fellowships carrying an annual stipend of $2,000 will be awarded each year at the annual meeting of the Board of Directors on the second Wednesday of March, beginning March, 1938. These fellowships will be awarded for a period of one year with the possibility of renewal up to three years.

2. When deemed necessary by the Board of Directors special grants of limited sums may be made to support the work carried on under a fellowship.

3. Applications must be on file at the office of the Secretary of the Foundation, Dr. William A. Fisher, Medical and Chirurgical Faculty Building, 1211 Cathedral Street, Baltimore, Maryland, on or before the first day of February.

4. Applications should be made upon blank forms which will be furnished by the secretary or by any member of the Board of Directors.

5. It is expected that at the end of his tenure each fellow will submit to the Board of Directors a summary of the results of his investigations.

The foundation is called the Finney-Howell Research Foundation, in honor of Dr. J. M. T. Finney, emeritus professor of surgery at the Johns Hopkins University, and Dr. William H. Howell, emeritus professor of physiology.

Members of the board of scientific directors are: Dr. Philip Bard, Dr. Curtis F. Burnam, Dr. John M. T. Finney, Dr. William A. Fisher, Dr. Wade Hampton Frost, Dr. William H. Howell and Dr. Warren Lewis, of Baltimore; Dr. Evarts A. Graham, of St. Louis; Professor E. L. Kenneway, of London; Dr. Jonathan C. Meakins, of Montreal, and Dr. Florence Sabin, of New York.

AWARD OF THE ROEBLING MEDAL OF THE MINERALOGICAL SOCIETY OF AMERICA TO DR. PALACHE

THE award of the Roebling Medal was authorized by the Mineralogical Society of America at the last annual meeting in Cincinnati, Ohio, in December, 1936. The medal is to be awarded for "meritorious achievement in mineralogy and allied sciences." It has been named in honor of the late Colonel Washington A. Roebling, of Trenton, N. J. Colonel Roebling was by profession an engineer, and in connection with his father, John A. Roebling, constructed many famous bridges throughout the country. However, his chief interest outside of his profession was mineralogy and he maintained an intense delight in it throughout his life. He built up one of the most complete private collections in the United States, and was so well acquainted with his specimens that, although he collected some 16,000 different mineral specimens, he was able to identify and describe them on occasion. His interest was not limited to the mere collection of rare specimens, but included the recent literature regarding them, and he often furnished specimens for research and analysis. His collection now forms part of the famous mineral display in the United States National Museum at Washington, D. C.

Colonel Roebling was a charter member of the Mineralogical Society and vice-president in 1924. His desire to see the society grow and enlarge was ever foremost in his mind, and led him to create an endowment fund to provide a wider scope in the publication of the journal of the society, the *American Mineralogist*. The medal bears the name of this distinguished patron of mineralogy in recognition of this service.

At its annual luncheon at the Hotel Washington, in connection with the annual meeting of the Mineralogical Society of America being held in Washington, D. C., from December 28 to 30, the society will present the Roebling Medal for the first time. Dr. Norman L. Bowen, president of the Mineralogical Society of America, professor of petrography at the University of Chicago, and a well-known authority on chemical mineralogy, will preside.

Dr. Edward H. Kraus, dean of the College of Letters and Science of the University of Michigan, formerly head of the department of mineralogy at that institution and one of the leading mineralogists in the United States, will present the Roebling Medal on behalf of the society to Professor Charles Palache, chairman of the department of mineralogy of Harvard University. The award is made in recognition of his outstanding contributions to the science of mineralogy.

Professor Palache has been generally recognized as the leading crystallographer in the United States. Chiefly through his crystallographic work, he has been instrumental in the determination of thirteen new mineral species recognized for the first time through his efforts.

One of Professor Palache's main contributions to mineralogy has been the description of minerals from Franklin, N. J., a mineralogically famous and industrially important zinc deposit. A large number of rare minerals has been found in the Franklin mines. In all, 160 different mineral species have been identified from this locality. No little part of this work has been accomplished by Professor Palache.

Apart from his numerous contributions in the field of pure science, Professor Palache has gained an

enviable reputation as a teacher, with a knack for arousing and sustaining the interest of his students. His ability to present the facts learned from his own researches has led students of mineralogy from many parts of the country to study with him.

PAUL F. KERR, *Secretary,*
Mineralogical Society of America

THE CHANDLER MEDAL AND LECTURE

THE Chandler Medal was presented to Dr. John Howard Northrop, member of the Rockefeller Institute for Medical Research, at Columbia University on October 27, and Dr. Northrop gave the lecture that is printed in the present issue of SCIENCE. Dean George H. Pegram, of Columbia University, introduced the Chandler medallist and lecturer in the following words:

This year the Chandler lecture carries added distinction as one of the events in celebration of the hundredth anniversary of the birth of Charles Frederick Chandler. Provision for the Chandler medal and the lecture by the medallist was the method chosen by friends of Professor Chandler to mark their admiration and affection for him by permanent provision for honoring those accomplishments in the wide field of chemistry that Chandler himself would most have praised and honored. Chandler took no narrow view of chemistry or the range of its services. He used jokingly to argue that whatever relates to anything composed of the chemical elements is properly chemistry, and there were those of us who believed that in his heart he was not joking. The growing list of Chandler medallists well reflects this Chandler breadth of view.

Since the presentation of the first medal to Professor Chandler in 1910, the recipients and the titles of their lectures have been as follows:

1914, Leo H. Baekeland, Some Aspects of Industrial Chemistry.
1916, W. F. Hillebrand, Our Analytical Chemistry and Its Future.
1920, Willis R. Whitney, The Littlest Things in Chemistry.
1921, Frederick G. Hopkins, Newer Aspects of the Nutrition Problem.
1922, Edgar F. Smith, Samuel Latham Mitchill—A Father in American Chemistry.
1923, Robert E. Swain, Atmospheric Pollution by Industrial Wastes.
1925, Edward C. Kendall, Influence of the Thyroid Gland on Oxidation in Animal Organism.
1926, Samuel W. Parr, The Constitution of Coal—Having Special Reference to the Problems of Carbonization.
1927, Moses Gomberg, Radicals in Chemistry, Past and Present.
1928, John Arthur Wilson, Chemistry and Leather.
1929, Irving Langmuir, Electrochemical Interactions of Tungsten, Thorium, Caesium and Oxygen.
1931, James B. Conant, Equilibria and Rates of Some Organic Reactions.
1932, George O. Curme, Jr., Synthetic Organic Chemistry in Industry.
1934, Jacob G. Lipman, The Stuff of Life.
1936, William F. Giauque, Temperatures Below 1° Absolute.

At the conclusion of the lecture Dean Pegram made the presentation of the medal and spoke as follows:

The Chandler lecturer of this centenary celebration will tell us of the aims, methods and significance of his researches in a region of discovery, into which he has opened trails and roads, on which others are welcomed and helped by him in further developments of the fertile fields of the complex protein molecules, that connect so directly with the processes that go on in living organisms.

It is with much pleasure and satisfaction that I introduce to you the Chandler medallist and lecturer of 1937, John Howard Northrop, member of the Rockefeller Institute for Medical Research. He will discuss for us the chemical nature and mode of formation of pepsin, trypsin and bacteriophage.

On the recommendation of the standing committee of faculty members on the Chandler medal, the Chandler medal for 1937 has been awarded by the trustees of Columbia University to John Howard Northrop in approbation of his successful and stimulating researches, notably various studies on fermentation, some leading to applications in the production of the useful solvents, acetone and ethyl alcohol, and more especially the isolation in purified and crystalline form of the digestive enzymes, pepsin and trypsin, and the parent proteins, or pro-ferments, from which pepsin and trypsin are formed, and his work on the kinetics of the destruction of bacteria by bacteriophage, on the conditions governing the production of bacteriophage, and his purification of a certain bacteriophage; a succession of researches which have opened up the way for himself and for others to reach a much clearer and more definite understanding of the properties of the complex protein molecules recognized as enzymes or pro-ferments or viruses, which play such an important part in the chemical reactions that go on in the processes of living organisms.

It is especially appropriate that on this Chandler centenary the recipient of the Chandler medal should be one of Professor Chandler's own students, one of his "boys," one whose father before him was one of Chandler's "boys" and later a member of the staff of the university; that he should be the great grandson of the man in whose memory the Columbia chemical laboratory, Havemeyer Hall, was given to the university; that he should be the recipient of four degrees, A.B. 1912, M.A. 1913, Ph.D. 1915, Hon. D.Sc. 1937, from Columbia; that he should once have been a Cutting fellow, and that he should already have been awarded the Stevens prize of our medical college.

The ties with Professor Chandler himself are strong with you, sir. I have the happy privilege of making them still more strong on this occasion by asking that this Charles Frederick Chandler medal of 1937 be placed in your hands by the one who stood closest to him, Mrs. Chandler herself.

MEDALLISTS AND OFFICERS OF THE ROYAL SOCIETY

THE following awards of medals have been made by the president and council of the Royal Society:

Royal Medals to Professor Nevil Vincent Sidgwick, F.R.S., in recognition of his distinguished, stimulating and continuous work on valency and on molecular structure, and to Professor Arthur Henry Reginald Buller, F.R.S., in recognition of his researches on the general biology and sexuality of the fungi.

The Copley Medal to Sir Henry Dale, F.R.S., in recognition of his important contributions to pharmacology, particularly to the pharmacology of muscle and of neuromuscular transmission.

The Davy Medal to Professor Hans Fischer, in recognition of his work on the chemistry of the porphyrins, particularly his determination of their detailed structure by degradation and his syntheses of porphyrins of biological importance.

The Buchanan Medal to General F. F. Russell in recognition of his work in relation to public health problems in many parts of the world on behalf of the International Health Division of the Rockefeller Foundation.

The Sylvester Medal to Professor A. E. H. Love, F.R.S., in recognition of his researches in classical mathematical physics, particularly the mathematical theories of elasticity and hydrodynamics.

The Hughes Medal to Professor Ernest O. Lawrence in recognition of his work on the development of the cyclotron and its application to investigation of nuclear distintegration.

The following is a list of those recommended by the president and council for election to the council of the Royal Society at the anniversary meeting on November 30:

Sir William Bragg, *president;* Sir Henry Lyons, *treasurer;* Sir Frank Smith and Professor A. V. Hill, *secretaries;* Sir Albert Seward, *foreign secretary.*

Other members of Council: Professor R. Whytlaw-Gray, Professor G. P. Thomson, Professor J. Proudman, Professor D. M. S. Watson, Dr. F. L. Pyman, Professor E. J. Salisbury, Professor S. P. Bedson, Professor M. Greenwood, Professor J. Mellanby, Sir Thomas Holland, Dr. G. T. Bennett, Professor J. Chadwick, Professor D. Keilin, Professor J. Graham Kerr, Sir Robert Pickard and Mr. H. R. Ricardo.

SCIENTIFIC NOTES AND NEWS

DR. CARL VOEGTLIN, in addition to his present work as chief of the Division of Pharmacology in the National Institute of Health, has been appointed by Surgeon General Parran as director of cancer research in the U. S. Public Health Service.

THE retirement is announced of Dr. Rudolf Ruedemann, New York State paleontologist. Dr. Ruedemann was appointed assistant paleontologist in 1899 and has been state paleontologist since 1926.

THE honorary degree of doctor of science was conferred upon Dr. Annie Jump Cannon, curator of astronomical photographs at the Harvard College Observatory, at the Mount Holyoke Founder's Day exercises, which marked the completion of the first hundred years of the college. Dr. Cannon made an address entitled "Stars over the Sea."

AT the August commencement of the Texas Technological College the honorary degree of doctor of science was conferred on Clifford Winslow Seibel in recognition of his researches on helium. Dr. Seibel is supervising engineer of the helium plant and cryogenic laboratory of the Bureau of Mines at Amarillo, Texas.

THE University of Sheffield has conferred the honorary degree of doctor of metallurgy on Dr. George B. Waterhouse, professor of metallurgical production at the Massachusetts Institute of Technology and president of the American Society of Metals. The degree was awarded *in absentia* at a recent congregation of the college.

AMONG the honorary degrees to be conferred by the University of Reading on the occasion of the installation of Sir Samuel Hoare as chancellor of the university on November 29 is the doctorate of science on Professor James Chadwick, director of research in radioactivity in the Cavendish Laboratory of the University of Cambridge, and on Sir Edward B. Poulton, formerly Hope professor of zoology at the University of Oxford, this year president of the British Association for the Advancement of Science.

THE Brewster Medal of the American Ornithologists Union "for outstanding ornithological achievement" during the year was awarded on November 17 at the Charleston meeting to Dr. Robert Cushman Murphy, of the American Museum of Natural History, for his work on "Oceanic Birds of South America."

KING LEOPOLD of Belgium decided several months ago to confer the Grand Cordon of the Order of Leopold on Guglielmo Marconi, but his death on July 20 occurred before this could be done. It will now be conferred posthumously. The insignia which the King intended to present personally to Marconi will be forwarded to his family through the Belgian Embassy in Rome.

THE Chicago Section of the American Chemical Society will hold a special meeting at the Stevens

Hotel on the evening of November 26 to celebrate the seventieth birthday of Professor Vladimir N. Ipatieff, director of chemical research of the Universal Oil Products Company and emeritus professor of chemistry at Northwestern University. There will be a dinner at 7:00 P. M., followed by a symposium in which Professor Ipatieff will participate on the general subject of catalysis and its rôle in chemistry. The program includes addresses by Professor Homer Adkins, of the University of Wisconsin, on "The Ipatieff Method of Hydrogenation," and by Thomas Midgley, Jr., vice-president of the Ethyl Gasoline Corporation, on "The Philosopher's Stone of To-day." Dr. Frank C. Whitmore, president of the American Chemical Society and dean of chemistry and physics at the Pennsylvania State College, will be the first speaker at the dinner. Introduced by H. J. Halle, president of the Universal Oil Products Company, Chicago, Dr. Ipatieff will make a brief response, "In Retrospect." The dinner will close with an epilogue by Dr. Harrison E. Howe, editor of the *Journal of Industrial and Engineering Chemistry*.

THE presentation to Dr. Thomas H. Norton of the Lavoisier medal of the Société Chimique de France was made at a meeting of the American section of the society at Columbia University on November 19. Comte de Ferry de Fontnouvelle, French Consul General, made the presentation, and Professor D. D. Jackson, head of the department of chemical engineering of Columbia University and president of the American section of the Société de Chimie Industrielle, described the life and accomplishments of the medalist, to which Dr. Norton responded. Dr. Norton was born in Rushford, N. Y., in 1851 and graduated from Hamilton College in 1873. He was professor of chemistry at the University of Cincinnati from 1883 to 1900 and had been connected with various chemical companies and had held various consulates and diplomatic positions. Since 1932 he has been on the technical staff of the American Cyanamid Company.

DR. E. P. SCHOCH, professor of chemistry and director of the Bureau of Industrial Chemistry at the University of Texas, was honored with a supper on November 9 by the San Antonio Manufacturers' Association. An embossed copy of resolutions in appreciation of Dr. Schoch's contributions to science and to the development of Texas was presented to him.

A PORTRAIT in oils of Dr. George B. Wallace, senior member of the faculty of the New York University College of Medicine, was presented to the college on November 15 on the occasion of the completion of his thirty-sixth year of active service in the institution. The speakers included Dr. Alfred N. Richards, professor of pharmacology at the University of Pennsylvania, who was chairman of the portrait committee, and Dr. Phoebus A. T. Levene, of the Rockefeller Institute for Medical Research. Dean Currier McEwen, of the College of Medicine, accepted the portrait for the college.

OFFICERS of the American Ornithologists Union, meeting in Charleston, S. C., on November 17, were elected as follows: *President,* Dr. Herbert Friedmann, biologist and ornithologist of the U. S. National Museum; *Vice-presidents,* Dr. James P. Chapin, of the American Museum of Natural History, and James Lee Peters, of the Museum of Comparative Zoology, Cambridge, Mass.; *Secretary,* Lawrence M. Hicks, of Columbus, Ohio, succeeding Dr. T. S. Palmer, of the Bureau of Chemistry and Soils, who has served as secretary for twenty years, and *Treasurer,* W. L. McAtee, of the U. S. Biological Survey. The council voted to hold the meeting in 1938 in Washington and the 1939 meeting in California.

AT the recent annual meeting in Washington of the Association of Land Grant Colleges and Universities the officers elected were: *President,* Dr. Cecil W. Creel, director of extension at the University of Nevada; *Vice-president,* Dr. J. A. Burruss, president of the Virginia Polytechnic Institute; *Secretary-Treasurer,* Thomas P. Cooper, of the University of Kentucky; *Members of the Executive Committee,* Dean O. M. Leland, University of Minnesota; President J. J. Tigert, University of Florida; President Charles E. Friley, the Iowa State College; President R. G. Bressler, Rhode Island State College; President C. A. Lory, Colorado State College; Dean F. B. Mumford, the University of Missouri; President T. O. Walton, the Texas Agricultural and Mechanical College, and Dean C. E. Ladd, Cornell University. Dr. R. A. Pearson, formerly president of the University of Maryland, and Dr. A. R. Mann, formerly provost of Cornell University, were elected life members of the committee.

AT the recent St. Louis meeting of the American Institute of Chemical Engineers, Frederick C. Zeisberg, of Wilmington, Del., was elected president. Other officers elected were: Dr. Webster N. Jones, dean of engineering, at the Carnegie Institute of Technology, Pittsburgh, vice-president; Stephen L. Tyler, of New York, secretary, and C. R. De Long, of New York, treasurer.

MEMBERS of the council of the Royal Society of Edinburgh have been elected as follows: *President,* Sir D'Arcy Wentworth Thompson; *Vice-presidents,* Professor F. A. E. Crew, Lieutenant-Colonel A. G. M'Kendrick, Principal J. C. Smail, Professor J. Walton, Dr. James Watt, Professor E. T. Whittaker; *General Secretary,* Professor James P. Kendall; *Sec-*

retaries to Ordinary Meetings, Dr. A. C. Aitken and Dr. C. H. O'Donoghue; *Treasurer,* Dr. E. M. Wedderburn; *Curator of Library and Museum,* Dr. Leonard Dobbin.

CARL L. BAUSCH, vice-president of the Bausch and Lomb Optical Company, has been elected a manager of the American Society of Mechanical Engineers for a three-year term beginning on December 10.

BECAUSE of continued illness Professor Margaret F. Washburn has retired from active teaching at Vassar College and has been made emeritus in psychology.

DR. OSCAR M. BALL, for thirty-four years professor and head of the department of biology of the Agricultural and Mechanical College of Texas, has retired from active teaching with the title professor emeritus. He will devote his entire time, as curator of the college museum, to his collections of fossil plants, and to the fossil vertebrata assembled by the late Dr. Mark Francis.

THE North Dakota State Board of Administration has appointed Dr. Earl A. Helgeson, associate professor of botany, to be acting head of the department of botany at the Agricultural College. He takes the place of Dr. Herbert C. Hanson, who is now acting director of the Experiment Station.

DR. MAXIMILIAN EHRENSTEIN, formerly at the University of Virginia Medical School, has been appointed assistant professor of chemistry in the School of Medicine of the University of Pennsylvania. Before coming to the United States he had been assistant to Adolf Windaus, Göttingen; Paul Karrer, Zurich, and Heinrich Wieland, Munich. Later he became privatdocent at the University of Berlin.

THE departments of botany of Cornell University and the University of Chicago have arranged an exchange of instructors for the winter quarter of the current academic year. Dr. R. A. Laubengayer, of Cornell, and Dr. Paul D. Voth, of Chicago, have been selected for the exchange. Both instructors will be engaged in the teaching of general botany in the large elementary courses.

RALPH R. BEAL, supervisor of television field tests for the Radio Corporation of America, has been appointed to the newly established position of research director of the company.

N. G. HUNTLEY, mapping officer of the Government of the Union of South Africa, recently spent about twelve days in Washington for the purpose of visiting the Geological Survey and other mapping agencies of the Federal Government. He plans to organize a mapping agency for his government following the best methods and practices that have proved their value in the United States and other nations on his itinerary.

C. W. GILMORE, curator of the division of vertebrate paleontology of the National Museum, gave an illustrated lecture on "Dinosaurs: How They are Collected, Prepared and Mounted for Exhibition" before a meeting of the Washington Academy of Sciences on November 8.

DR. HAROLD SCOTT delivered the FitzPatrick lectures of the Royal College of Physicians, London, on November 9 and 11. His subject was "Conquest of Disease in the Tropics."

THE ninth International Ornithological Congress will be held at Rouen from May 9 to 13, 1938, under the presidency of Professor Alessandro Ghigi, professor of zoology at the University of Bologna.

THE thirty-ninth annual meeting of the American Physical Society will be held at Indianapolis, Ind., on Tuesday, Wednesday and Thursday, December 28, 29 and 30, in affiliation with Section B, physics, of the American Association for the Advancement of Science. The preliminary arrangements include a joint session on Tuesday, December 28, with Section B of the American Association and the American Association of Physics Teachers, at which time the retiring vice-president of Section B, Physics, Dr. George B. Pegram, of Columbia University, will deliver an address. There will also be an address by the president of the American Physical Society, Dr. H. M. Randall, of the University of Michigan, on "The Spectroscopy of the Far Infrared," and one by Professor G. Breit, of the University of Wisconsin. The dinner will be held on Wednesday, December 29, at the Athletic Club.

THE seventh National Symposium for Organic Chemistry of the American Chemical Society will be held at Richmond, Va., on December 28, 29 and 30, under the auspices of the Division of Organic Chemistry and of the Virginia Section. Registration and all meetings will be held in the John Marshall Hotel. The speakers will include: W. E. Bachmann, University of Michigan; P. D. Bartlett, Harvard University; M. Bergmann, the Rockefeller Institute; R. Connor, University of Pennsylvania; A. Corwin, the Johns Hopkins University; Wm. L. Evans, the Ohio State University; H. B. Hass, Purdue University; A. L. Henne, Midgley Foundation; C. D. Hurd, Northwestern University; R. E. Marker, the Pennsylvania State College; S. M. McElvain, University of Wisconsin; E. Mosettig, University of Virginia; A. A. Morton, Massachusetts Institute of Technology; C. R. Noller, Stanford University; A. Russell, Röhm and Haas Company; L. I. Smith, University of Minnesota; R. R. Williams, Bell Telephone Research Lab-

oratories. An evening session dealing with the application of micro- and semimicro-methods to research in organic chemistry will be held on the evening of December 28. An apparatus exhibit devoted to micro- and semimicro-apparatus is also being arranged. An informal dinner is planned for Wednesday evening.

THE annual two-day Ohio-Michigan regional meeting of the American Chemical Society took place at Columbus, Ohio, on November 19 and 20. Twenty-two papers reporting scientific advances in industrial and university laboratories were presented. An address on "Broad Trends in Chemical Research" was made by Dr. E. R. Weidlein, director of the Mellon Institute of Industrial Research and president of the American Chemical Society. The Ohio State University, the Battelle Memorial Institute and the Columbus Section of the society sponsored the assembly, to which the Ohio, Michigan, Kentucky and the Kanawha Valley Sections of the society, comprising a membership of 2,000, sent delegates. The technical sessions on Friday were held at the Ohio State University, and on Saturday morning a session was held at the Battelle Memorial Institute. At the annual dinner Dr. Weidlein was the principal speaker. Professor Harold S. Booth, of Western Reserve University, showed motion pictures of leaders of American chemistry at work. There were inspection trips through the laboratories of the Ohio State University, the Battelle Memorial Institute and the Owens-Illinois Glass Company in Newark, Ohio, on Saturday afternoon. The offices of *Chemical Abstracts*, under the direction of Professor Evan J. Crane, were also visited.

To provide opportunity for discussion of road and transportation problems, the seventeenth annual meeting of the Highway Research Board of the National Research Council will be held in Washington, D. C., for four days, from November 30 to December 3, instead of for the two days that formerly were found sufficient. A large part of the time will be devoted to open departmental meetings on economics, design, materials and construction, soils investigations and roadside developments. On Tuesday, November 30, the meeting of the Department of Soils Investigations will be held and on Wednesday morning papers and reports relating to soils and maintenance will be presented. Wednesday afternoon will be devoted to materials and construction and roadside development. Thursday's meetings will include a general session in the morning on finance, materials and construction and roadside development and one in the afternoon on highway safety. Friday will be devoted to design and economics.

APPROXIMATELY two hundred physicists of Upper New York State met on November 6 at Cornell University for a program of scientific papers and a business organization meeting. It was estimated that about forty per cent. of those present were teachers in colleges and universities, twenty per cent. high school teachers and forty per cent. from industry. It was unanimously voted to form an organization to be known for the present as the Physics Association of Upper New York State. No officers were elected but the affairs of the organization were placed in the hands of a Committee on Organization and Arrangements made up as follows: G. H. Cameron, Hamilton College; H. P. Gage, Corning Glass Works; R. C. Gibbs, Cornell University; L. G. Hector, University of Buffalo, and P. I. Wold, Union College, *chairman*. There was discussion as to whether it would be more advantageous to operate this association as an entirely independent organization or to seek affiliation with one of the existing national societies in the field of physics. The opinion was definitely in favor of the latter course.

THE Committee on Scientific Research of the American Medical Association has made a grant to Washington University School of Medicine to aid Dr. Martin Silberberg in his work on the influence of hormones on bone growth. This research is being carried out under the direction of Dr. Leo Loeb in the department of experimental pathology.

THE California Institute of Technology has been made the chief eventual beneficiary in the estate of Henry M. Robinson, a trustee of the institute, who died in Pasadena on November 3. The will provides that the residue of the estate, which is valued at $800,000, after individual bequests have been provided for, shall be placed in trust for his widow, and that at her death the entire estate shall go to the institute.

DISCUSSION

FREEDOM OF THE PRESS AND THE SCIENTIST

FREEDOM of speech and of the press are privileges dear to the American, but do we not too frequently abuse these privileges as we do various other liberties upon which it has become necessary to impose restrictions? The chief restriction on the scientist's publication is the publisher's profit or the bank balance of the technical society. An editor, to be sure, may reject an article for other reasons, but the author may publish at his own expense without regard to the contents.

I am quite aware of the need of increased facilities for publication, but I am convinced that we have a still greater need for a wiser use of those now available. The worker of to-day is confronted by an array of past publications vastly greater than that of a single generation before. It has been an almost hopeless struggle for abstracting and indexing to keep pace with the output. Should we not give more attention to these difficulties at their beginnings rather than merely satisfy our present wishes and let the future care for itself? The concentration of related subject-matter is a problem frequently considered, but the multiplication of small overlapping journals seems much more popular.

Some journals carry a large number of brief notes representing a quantity of detailed information "placed on record." These require an entirely undue amount of indexing and are practically useless without it. Surely they would be more satisfactory if compiled in some orderly fashion. Surely some of them are scarcely worth publishing and others might well be delayed for more effective presentation. Some authors seem to have a penchant for publishing in as many different journals as possible and thus scatter brief notes on a single topic. I have a special grievance against the short articles which state that a more complete account is being published (or will be) elsewhere. A well-known editor tells me that a large part of these never appear. Sometimes they are designed to merely call attention to work in progress and solicit cooperation and may be commendable. Often they give preliminary results, describe a new species or merely mention it without description. There seems little excuse for cluttering up the journals with these fragments.

A few years ago I sent a circular letter with similar suggestions to about one hundred biologists, including officers of several national societies and editors of their journals. The majority of the comments were favorable. As one put it, "When it comes to publication, we scientists certainly are unscientific." One taxonomist suggests that it would be desirable to have all descriptions of new forms published in revisionary treatments, but that the new forms are continually coming to light and that no revisionary work on the group is under way. As a matter of fact there seems a distinct tendency to describe the new forms in advance of other publication. Sometimes this is to avoid the introduction of such material into a general catalogue or manual in which brief and uniform treatment is essential. In other cases the original descriptions are closely followed by a general treatment (usually in a different journal) and it seems a question whether any gain is achieved.

In some quarters it seems much easier to secure funds for mimeographing than for ordinary printing, thus resulting in a quantity of preliminary reports and a lack of substantial publication. It seems unfortunate that it is so easy to secure publication of brief notes or short articles and so difficult to care for the longer articles. Some progress has been made in recent years through the establishment of several publications designed especially for the latter group. We make little, if any, advance in handling those of the first sort. I would be disposed to accept the present conditions as necessary if it were not for the frequent encounters with articles which seem quite an unnecessary burden upon our limited publication space. We could profit by closer contact and cooperation in preparing the results of our investigations. Is delay in publication always so serious as it seems? Is it not possible to have more editorial supervision, especially along the line of contacting other workers?

One objection to delaying and to incorporating results with those of other workers is the possible loss of credit. Publications are one of the worker's chief assets. To have prepared something for presentation is indeed an accomplishment, but it is well known that too often an employer is concerned with a list of papers rather than with the worth of their content. If we can secure judgment based upon quality rather than quantity, we shall have gone a long way toward the improvement of publications. If the field of publication is limited, surely we should endeavor to utilize it to the best advantage. The investigator has a real duty to humanity by presenting his material so that it will be of greatest service.

O. A. STEVENS
NORTH DAKOTA AGRICULTURAL COLLEGE

ARCHEOLOGY AS A TOOL FOR USE IN PREDICTING THE PERMANENCY OF AGRICULTURE

IN a recent issue of SCIENCE[1] the results of the excavations in Kansas and Nebraska by Dr. Wedel were reported. He explained the alternation of agricultural and hunting phases in the prehistory of the central Great Plains as being caused by a corresponding alternation of humid and drought periods. During the more humid years agriculture was successful, but it could not maintain the people throughout an extended series of dry seasons.

Similar conditions to those found by Dr. Wedel in Kansas are to be found in the extreme southwestern portion of the Great Plains. East of the White Mountains in southeastern New Mexico are many sites of a lost group of the agricultural Pueblo peoples. Their fields were waste lands and their houses rubble-heaps when the Spanish entered the land; only wandering bands of hunters lived there then. Why did the little

[1] SCIENCE, 86: 2232: Supplement, 8–9, 1937.

shifting hunting camps replace the populous Pueblo villages? In an attempt to answer this question the writer has visited numerous sites in this and adjacent regions during the past three summers, studying the water supply, soil characteristics, topography and artifacts of each. From the pottery, which is being classified by the system of Dr. Mera of the Laboratory of Anthropology, a relative dating scheme is being developed for the times of settlement and abandonment of each of the sites.

The agricultural sites were of two types; those east of the Pecos River were in the rolling sandy prairie lying between the gypsum steppe, which borders the river, and the dunes of the Mescalero Sands further to the east; while the sites west of the Pecos were all in the alluvial bottoms of the small streams which flow eastward from the mountains. No agricultural sites were found or heard of on either the hard dry steppe or on the alkali flats of the Pecos. In general the sites are in locations which have in recent times been found to be the most suitable for agriculture. The use of deep wells has extended the range of arable land beyond that available to the Indians. Dry farming was practiced by the Pueblos on the sandy prairie, while they probably irrigated their stream bottom sites. It appears likely that the Pueblo people settled the entire region within the space of but a few years, but they abandoned the sandy lands long before they left their irrigated gardens beside the streams.

The abandonment of the sandy land sites was probably caused by the blowing of the soil, rather than by the pressure of nomadic tribes. At every site in the sandy lands there was ample evidence of wind-disturbed soil. Usually the soil was blown up into great dunes. Artifacts were abundant in the blows and part way up the windward sides, but were not to be found on the tops of the dunes. At a few sites the top-soil appeared to have been completely swept away, leaving only hard red barrens. Similar types of wind erosion are to be seen in the vicinity as the result of twentieth century mis-farming practices. Natural reclamation of such disturbed soil is extremely slow. Even though these blown-out fields have lain fallow for more than seven hundred years they are still barren wastes.

The irrigated sites in the valleys on the contrary show no evidence of permanent damage to the soil. Many such sites are now in cultivation, with no apparent signs of decadence. The earliest dwelling sites of the Pueblos along the little streams were on low ground by their gardens. There was no evidence of any regard or precautions for defense at these or the sandy land sites. They occupied these open sites in the Hondo valley somewhat later than the villages on the sands east of the Pecos. This peaceful period came to an end, and the final phase of this culture was when they commenced building pueblos on the high, steep and rocky hills overlooking the Hondo in a manner closely resembling the Piro towns of Gran Quivira and Loma Pelada a hundred miles to the northwest. The final abandonment of the valley sites appears to have been the result of the pressure of the nomadic tribes rather than that of a series of crop failures. There is some evidence that the people were weakened physically, and possibly in numbers, too, by mineral deficiencies in their diet.

These archeological findings are in quite close accord with the present trends of agriculture in this far corner of the Great Plains, thereby giving some confirmation to the theory of Dr. Wedel that archeology can assist in predicting the permanency of agriculture in many regions.

MAX C. MARKLEY

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CELL SHAPE PHENOMENA INTERPRETED IN TERMS OF COMPRESSED LEAD SHOT

THE shape of parenchymatous cells such as those found in the pith of vascular plants is undoubtedly the result of several factors, among which contact and pressure, the plane of cell division, cell elongation and varying adjustments among all these may each play a part.

In an attempt to determine the effect of contact and pressure on the shape of uniform spheres, small lead shot which had been selected for uniformity were used. The shot were poured into a cylinder and compressed at various pressures.[1] In one test sufficient pressure was used to eliminate all the air spaces between the spheres. A study of over five hundred of these compressed balls, omitting the peripheral layer adjacent to the wall of the cylinder, gave an average of 14.17 contacts or faces per ball. In another test somewhat less pressure was used, all the spaces between the spheres were not eliminated, and the average for the hundred balls examined was 12.9 contacts. Still less pressure gave an average of 11.0 contacts for one hundred balls; and slight pressure, just sufficient to cause flattening at the points of contact between adjacent spheres, gave an average of 8.4 contacts for the hundred balls examined.

These results indicate that when lead balls are poured into a cylinder there is an irregular distribution of contacts between spheres, and the "cannon ball" stacking, in which every sphere is in contact with twelve other spheres, does not occur. This irregular

[1] The compressions were made possible through the courtesy of the Civil Engineering Materials Testing Laboratories of Columbia University.

arrangement of contacts is maintained as the number of contacts becomes increased from 8.4 to 14.17, with additional pressure.

Lewis[2] has shown that the cells of the elder pith have an average of fourteen facets, and he emphasizes the orthic tetrakaidecahedron as a possible fundamental shape in such tissues. None of the orthic tetrakaidecahedra of Lord Kelvin, with eight hexagonal and six square faces, were found among the lead balls examined; however, when all the spaces between the shot were eliminated, the average number of contacts was very near fourteen. A less regular tetrakaidecahedron was formed, having in addition to hexagonal and square faces a relatively large number of pentagonal sides. This shows that the regular arrangement of spheres necessary to form the orthic tetrakaidecahedron of Lord Kelvin on compression was not present when the shot were merely poured into the cylinder. It also helps to explain the occurrence of pentagonal faces in the cells of elder pith found by Lewis.

That contact and pressure must be of marked importance in the determination of the number of faces occurring on parenchymatous cells seems obvious from the above experiments. It is further highly probable that the occurrence of intercellular air spaces in parenchymatous and other tissues is correlated with contact and pressure relationships. On the basis of contact and pressure alone, fewer contacts between adjacent cells would be expected in tissues with abundant air spaces.

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HABITAT OF OPHIOSAURUS VENTRALIS

Two specimens of *Ophiosaurus ventralis* were discovered in Cumberland County and one specimen in Buckingham County, Va., in September, 1937. The first two specimens had been killed on the highway by automobiles; the third one was captured and is now in the possession of the farmer who found it in Buckingham County. The distance from the most eastward to the most westward of these finds was about twenty miles. These counties are in Piedmont Virginia, about seventy-five miles north of the North Carolina line and 150 miles west of the Chesapeake Bay.

Since Ditmars places the Northern limit of this reptile in the eastern part of the United States as North Carolina, and Jordan as "to Virginia," it seems that these are the first recorded specimens for this section of the country.

W. A. BRUMFIELD

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FARMVILLE, VA.

[2] F. T. Lewis, *Proc. Am. Acad. Arts and Sci.*, 58: 537–552, 1923.

FRESH-WATER MEDUSAE IN VIRGINIA

FOURTEEN miles south of Lynchburg, in Crystal Lake on the James Wamble estate, gonosomes appeared in large numbers about August 5, and have been observed there at frequent intervals to the present (September 29). Vertical migrations of the medusae have been noted, showing no observed correlation with temperature, sunlight, wind or time of day. Sometimes the top meter of water over the greater part of the pond showed jellyfish actively swimming about. As many as 70 fair- to large-sized specimens have been counted in each cubic meter of water on such occasions. On other days, few medusae were seen except in the wake of the boat or where the water had been stirred to some depth by means of a paddle. A few triradiate and quinqueradiate specimens were collected. The average catch (quadriradiate) measured considerably larger than fresh-water medusae hitherto reported, some reaching a diameter of 22 mm. Otherwise the descriptions given for *Craspedacusta ryderi* (Potts) fit well enough. The reflexed, upstretched, long tentacles seem highly characteristic of even small specimens. All appear to be females. Parts of the lake where the depth is greater than two meters are well populated with medusae; between one and two meters they are less common, and in less than one meter of water they are rare. The water temperature at present is about 24° C. The water has a high organic content, and the bottom where shallower than two meters is densely covered with Utricularia. A green Stentor and a Spirostoma were very conspicuous protozoans occurring there in great numbers. The pond is created by an earthen dam which restrains a very small stream, and has been in existence some ten years. The pond was stocked with fingerling bream and black bass two years ago. Eels have been caught there, although the emptying stream is very small and quite shallow. The plant growth was largely cleared out last year. A search for hydroids was unsuccessful.

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SCIENCE AND DEMOCRACY

HAVING read the quotations from the New York *Times* in SCIENCE of Friday, October 22, entitled "Science and Democracy," I could not help but follow the urge to write my views on the subject.

I certainly admit with the author that freedom of thought and expression is in peril. In the totalitarian states the ruling dictators are going to see that this condition continues. But, I do not believe

that salvation of international democracy of science and of its objective lies in a world-wide organization. Energy put into such an organization is probably desirable if those contributing this energy do not use it all up in world-wide organization. I believe that a much larger amount of energy put into national organization would be justified, both here and in Great Britain, the only two remaining strongholds of democracy. If these strongholds can be fortified and maintained, there will be rallying places that will ultimately be the means of saving science. Charging out into the enemy's country when our own fortresses are being weakened, I believe is not the most satisfactory solution of the difficulty. By putting and keeping our own house in order, I believe that most can be accomplished for our foreign brethren.

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THE AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

MEETING OF THE EXECUTIVE COMMITTEE

AT the autumn meeting of the Executive Committee, held in Washington, D. C., on October 30 and 31, Drs. Cattell (*chairman*), Birkhoff, Caldwell, Chamberlin, Compton, Conklin, Livingston, McKinley, Moulton and Ward were present. A great deal of time was given to considering such matters of general policy as changing emphasis in the aims of the association and the character of its meetings, methods of extending its membership and influence, the promotion of broad symposia, the function of branches of the association and the use of the radio. Although these discussions did not crystallize into final form for recommendations to the council, they contained the promise of possible important developments in the work of the association.

MEMBERSHIP

At September 30, 1937, the total membership of the association was 18,303, of whom 744 were in arrears on their dues for one year and 490 for two years. During the fiscal year ended September 30, 1937, the membership of 528 persons lapsed for non-payment of dues, 355 members resigned from the association, and 198 members died. During the same period 35 members were reinstated and 1,107 new members were elected. Thirty-nine members became life members upon the payment by each of them of $100 to the association. The office of the permanent secretary sent out 37,754 letters for the purpose of obtaining new members. Heretofore all memberships of the association began as of October 1; henceforth, by vote of the executive committee, they may begin as of the first of any month.

FINANCIAL

Although the financial reports of the permanent secretary and the treasurer of the association are subject to audit, certain provisional figures may be presented now. The total income of the office of the permanent secretary for the fiscal year October 1, 1936, to September 30, 1937, was $86,541.86. The total expenses of the office of the permanent secretary were $84,647.99, of which $52,083.49 was for subscriptions for journals for members (including foreign postage), leaving a net balance of income over expenses of $1,893.87, or about 2.2 per cent. of the total income. The net expense of the Atlantic City meeting was $1,133.59, and of the Denver meeting, $3,763.95. The net profit to the association of the scientific exhibit at Atlantic City was $1,817.68.

The treasurer of the association reported cash receipts from all sources of $20,447.66 and total cash disbursements of $16,650.39. The cash balance of the treasurer at the beginning of the fiscal year was $15,524.43 and at the close of the year was $19,321.71. The treasurer reported that total assets of the association at the close of the fiscal year amounted to $271,087.07, of which $19,321.71 was in cash and the remainder in securities and mortgages. Of the latter, $108,836.45 was in endowment funds for promotion of scientific research.

The budgets of the office of the permanent secretary and of the treasurer were referred to the council with the approval of the executive committee. The executive committee appropriated to the Committee on Grants the sum of $2,000 for allotments in aid of research, and enough from the funds available for the purpose to make allotments for research through the state academies of science in accordance with methods heretofore in use.

ITEMS RELATING TO FUTURE MEETINGS

Indianapolis Meeting: The problem of the nomination of fellows of the association was referred to the Secretaries' Conference for consideration. The permanent secretary was authorized to have printed complimentary tickets for admittance to the general sessions of the association and to the exhibits. The appointment of the prize committee was placed in the hands of Professor F. K. Richtmyer (*chairman*) and the permanent secretary. It was voted that a suitable diploma be provided to accompany the $1,000 prize.

Ottawa Meeting: Dr. Ward was appointed to repre-

sent the officers of the association in working out with the Ecological Society of America a symposium for the Ottawa meeting. Other suggestions for cooperating with Canadian scientists for the purpose of developing a strong program were approved.

Richmond Meeting: Dr. McKinley presented the plans developed by Dr. Walter L. Treadway, Assistant Surgeon General of the U. S. Public Health Service, for a symposium on mental health. The executive committee approved the plans and invited Dr. Treadway to organize and take charge of the symposium, with the assistance in administrative details of the secretary of the Section on Medical Sciences.

Milwaukee Meeting: The dates set for the Milwaukee meeting were June 19 to 24, 1939.

Miscellaneous Reports

Dr. Harvey Fletcher, who was the representative of the association at the Nottingham meeting of the British Association for the Advancement of Science, sent in an interesting report on the methods of our English cousins of conducting general scientific meetings. He commented particularly and approvingly of the interesting general addresses and the enjoyable social functions. Dr. Caldwell presented a report by Dr. Harry A. Carpenter, who represented the association at the Tokio, Japan, Conference of the Science Section of the World Education Federation. Dr. Caldwell was directed to express to Dr. Carpenter the appreciation of the executive committee for representing the association at the Tokio meeting. Dr. Caldwell made a report on plans for weekly broadcasts on science under the auspices of the association, and the permanent secretary was authorized to attempt to put the plans into effect. Dr. Caldwell reported on the Indianapolis program of the American Science Teachers Association and also on the formation of branches of the association. A report from Dr. Gregory D. Walcott, chairman of the Committee on Source Books, was presented; the permanent secretary was directed to express to the committee the association's appreciation of the splendid progress made.

Appointments of Representatives

Dr. Ward was appointed the representative of the association in any group discussions pertaining to the Rocky Mountain Tunnel Project. Dr. Malcolm H. Soule was appointed the representative of the association at the Third International Congress for Microbiology, to be held in New York City in the summer of 1939. Dr. Franz Boas was appointed the representative of the association at the International Congress of Anthropology and Ethnology, to be held in Copenhagen, Denmark, from August 1 to 6, 1938. Dr. Selskar M. Gunn and Dr. Reginald R. Gates, of the University of London, King's College, were appointed representatives of the association at the twenty-fifth session of the Indian Science Congress, to be held in Calcutta, India, from January 3 to 8, 1938.

Miscellaneous Actions

The executive committee voted that the inscription on the medal accompanying the Theobald Smith Award, the first of which is to be presented to Dr. Robley D. Evans at Indianapolis, shall be: "Awarded in (year) to" on the first line, with the name of the recipient immediately below. Following the report that the bibliography on "Conserving Our Natural Resources" is now ready for free distribution, the executive committee passed a vote of thanks and appreciation to Dr. Joseph Wheeler, Chairman of the Committee on Popular Science Reading Lists. Three fellows were elected upon recommendations of the Sections on Physics and Medical Sciences. The Association for Symbolic Logic, having 196 members, of whom 48 are members of the association and 32 are fellows, was admitted to the relationship of an affiliated society. The executive committee voted its appreciation to Dr. W. W. Campbell for his letter on general operations of the association, in which he expressed the opinion that two meetings per year are inadvisable and that the programs should have more general papers and fewer that are narrowly technical.

F. R. Moulton,
Permanent Secretary

SPECIAL ARTICLES

THE NATURE OF PAPAIN ACTIVATION

Among the enzymes that digest high molecular proteins and therefore are designated proteinases, the papainases distinguish themselves by the property of being activated in the presence of SH compounds or of HCN. This activation was considered for some time to be due to a reduction process.[1] Doubts regarding this interpretation arose when it was discovered that activated papain is capable of digesting simple substances such as hippurylamide[2] and that this digestion can be activated and inhibited by processes which can scarcely be regarded as reductions and oxidations. Thus the hydrolysis of hippurylamide or of carbobenzoxyisoglutamine was inhibited by phenylhydrazine, while the digestion of albumin peptone was activated by the same reagent.[3] This contrasting

[1] T. Bersin, *Ergebnisse der Enzymforschung*, 4: 68, 1935.

[2] M. Bergmann, L. Zervas and J. S. Fruton, *Jour. Biol. Chem.*, 111: 225, 1935.

[3] M. Bergmann and W. F. Ross, *Jour. Biol. Chem.*, 114: 717, 1936.

behavior toward two substrates led to the hypothesis that papain and other papainases are constituted of two partial enzymes which are inactive when associated with each other, but which dissociate in the presence of activators and thus become active.[4]

The experimental basis of this hypothesis seemed unsatisfactory because of the heterogeneous nature of albumin peptone which was employed as one of the substrates. This peptone is a mixture of various protein split-products and frequently contains substances which may influence the activity of the enzyme. We have now found that data similar to those obtained with albumin peptone can be gotten with a well-crystallized synthetic substance, benzoyl arginine amide. The hydrolysis of this synthetic compound is activated by the addition of phenylhydrazine. However, this activation is observed only if the papain preparation is a natural, unpurified extract which contains SH compounds as natural activators. Addition of phenylhydrazine to purified papain, in which these accompanying activators are absent, produces no activation towards either albumin peptone or benzoyl arginine amide. Addition of HCN or a similar activator to the purified papain is necessary to restore the activation by phenylhydrazine (Table I). A similar effect was

TABLE I
ACTIVATION OF PAPAIN BY VARIOUS REAGENTS

Enzyme preparation	Substrate		
	Albumin peptone	Benzoyl arginine amide	Carbobenzoxyisoglutamine
Natural papain	.04	.01	.09
Natural papain + phenylhydrazine	.26	.33	.05
Purified papain	.00	.02	.03
Purified papain + phenylhydrazine	−.02	−.03	.03
Purified papain + phenylhydrazine + HCN	.65	.16	.01
Purified papain + phenylhydrazine + cysteine		.60	.48

The splitting is expressed as the increase in cc of 0.01 N KOH per 0.2 cc of the reaction mixture. An increase of 1 cc for the synthetic compounds corresponds to 100 per cent. splitting of one peptide linkage. Time interval, 24 hours. Temperature, 40° C. pH, 5.0.

reported[5] for the splitting of carbobenzoxyisoglutamine where the presence of a large concentration of cysteine effected an activation of purified papain + phenylhydrazine. These experiments tend to show that in the behavior of papain toward various substrates there is no absolute differentiation but rather a relative one which depends upon the nature of the substrate. In view of this finding, the hypothesis of a two-enzyme system in papain becomes at present superfluous.

[4] M. Bergmann and J. S. Fruton, SCIENCE, 84: 2169, 1936.

[5] M. Bergmann, J. S. Fruton and H. Fraenkel-Conrat, *Jour. Biol. Chem.*, 119: 35, 1937.

Synthetic substrates were also used to study the effect of several purification procedures on the activity of papain. It was observed that essentially all the proteolytic activity toward both gelatin and carbobenzoxyisoglutamine is precipitated between 0.5 and 0.7 saturation with respect to ammonium sulfate.[6]

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OSMOTIC EFFECTS OF DEUTERIUM OXIDE (HEAVY WATER) ON LIVING CELLS

IN considering the permeability of erythrocytes to D_2O[1] it occurred to me that D_2O, because its vapor pressure was less than that of H_2O, would cause osmosis in the same way that concentrated solutions would. The vapor pressures[2] of D_2O and H_2O were 15.06 and 17.36 mm respectively at 20°, and H_2O in a 7.43 M ideal solution would have a vapor pressure equal to that in pure D_2O, *i.e.*, 15.06 mm. In this case we might suppose that the rate of osmosis is roughly parallel to the difference of equilibrium vapor pressures, *i.e.*, fugacities of the two types of water. I have found that plasmolysis of plant cells and hemolysis of erythrocytes occurs, although osmosis is so transient that in my experiments hemolysis is incomplete, and plasmolysis is expressed only by shrinkage of cell and cell wall together.

I have studied the shrinkage preceding plasmolysis in *Nitella clavata* A. Br., using a method used by Collander and Bärlund[3] for penetration of alcohol into similar material, *Chara*. We have isolated terminal "leaves" 5–12 mm long, attached to a node, and left them in double distilled water for about a day to recover. A leaf was fixed by dropping wax (3 parts cacao, 1 beeswax) on the basal end, meantime supporting the free end with wet filter paper, in a glass cell 20 × 6 mm, and 4 mm deep. About 0.4 ml of water was put in, and the filter paper removed. The cell was put on a mechanical stage under a 16 mm objective (Bausch and Lomb) and No. 8 periplan (Leitz) oculars containing an ocular micrometer. One of the divisions of the scale of this micrometer measured 7.2 μ in the focal plane. Using 1 ml pipettes water was removed and replaced several times to make sure of the regular behavior of the leaf. When the leaf

[6] A. K. Balls, H. Lineweaver and R. R. Thompson (SCIENCE, 86: 379, 1937), used this property for the isolation of papain crystals.

[1] S. C. Brooks, *Jour. Cell. Comp. Physiol.*, 7: 163–171, 1935.

[2] G. N. Lewis and R. T. MacDonald, *Jour. Am. Chem. Soc.*, 55: 3057–59, 1933.

[3] R. Collander and H. Bärlund, *Acta bot. Fenn.*, No. 11, 1–114, 1933.

regularly came back immediately to the same zero on the micrometer after each change with no change in length, D_2O[4] was now introduced in the same way. Observations were made, and when shrinkage and recovery were completed, D_2O was replaced with H_2O and observations again made. This was repeated for D_2O and usually also for H_2O. Fig. 1 shows the

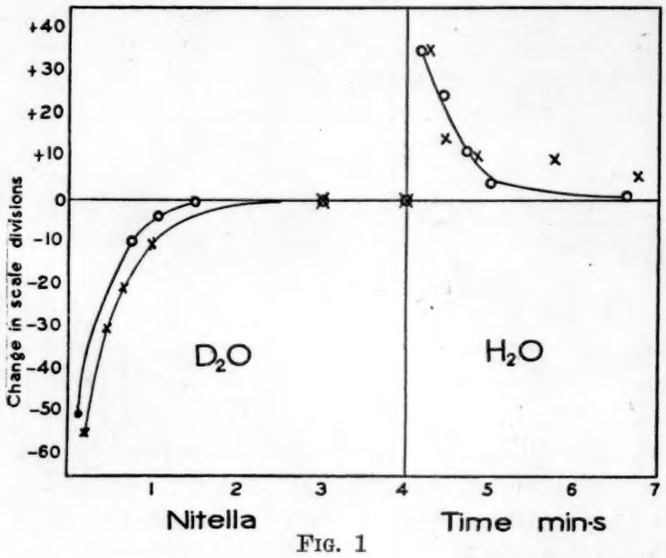

FIG. 1

changes in micrometer divisions, showing shrinkage after application of D_2O, followed by recovery (*i.e.*, swelling) to the original length, while on applying the H_2O, after D_2O, the filament first elongated and then returned to the original length. Altogether six tests for D_2O and five for H_2O were made. All experiments gave the same general behavior, but there was failure of the leaf to return to zero in some cases, either because of slipping of the attachment or the mechanical stimulation by bending against the sides of the glass cells. Observations in D_2O were made for 2 to 11 minutes, and in H_2O for 4 to 12 minutes.

The leaves of *Nitella* shrank 0.60–1.37 per cent. in D_2O, and elongated 0.40–0.70 per cent. in H_2O. These values were observed as nearly as possible at 5 or 10 seconds. The process of putting the water in the glass cell occupies 2 to 4 seconds. Even before the leaf appeared in the microscope field it had passed through a maximum, and by the time observation was made it was already returning toward zero. By this method the true maxima could not be observed, and since the whole recovery occurred in about 1 minute in D_2O, the time recorded in the earlier observations were actually only approximately measured. One notes that D_2O acts as a plasmolytic agent, although plasmolysis is concealed by the stretched elastic cell wall which follows the shrinkage. H_2O causes swelling of the cell, the counter change of that produced by D_2O.

It should be possible to make such cells as erythrocytes to swell on return to an H_2O solution from an equally concentrated D_2O solution, thus causing hemolysis. This is analogous to hemolysis caused by treating erythrocytes with hypotonic solutions, since H_2O is hypotonic to D_2O. We have tried using D_2O and H_2O solutions in 1.1 per cent. or 0.8 per cent. NaCl. Erythrocytes were obtained by centrifugation from 0.2 ml of defibrinated sheep blood. In the first experiment 1.1 per cent. NaCl solutions were used. In the second experiment 0.8 per cent. NaCl solutions were used, and the sediment was first washed in H_2O–NaCl solution by centrifugation and decantation. After that in both cases the erythrocytes were suspended in 1.0 ml of D_2O–NaCl, allowed to stand for 10 minutes, then centrifuged, and the D_2O–NaCl decanted, the decantate saved. The sediments were suspended in 5.0 ml of corresponding H_2O–NaCl solutions (1.1 and 0.8 per cent. respectively). Hemolysis was shown by the discolored supernatant fluids decanted after suspension and centrifugation. The remaining erythrocytes were hemolysed in 5.0 ml of pure H_2O. In the first experiment about 22 per cent. of the hemoglobin was in the H_2O–NaCl fluid, as compared with 78 per cent. in the fluid from the last sediment of cells. In the second experiment colorimetric measurements showed that the H_2O–NaCl solution contained 38.7 per cent. of the hemoglobin, 61.3 per cent. in the final sediment. The decanted D_2O was not perceptibly discolored.

The erythrocytes suspended in a D_2O–NaCl solution take up D_2O. These cells would have a vapor pressure much lower than that of the H_2O–NaCl, the H_2O in a few seconds enters the cells and this swelling brings hemolysis of the weaker part of the erythrocytes. Here again D_2O is hypertonic to H_2O and is an active osmotic agent.

The osmotic effects of D_2O as compared to H_2O produce some of the well-known phenomena associated with biological effects. The press, for example, mentioned the "burning sensation" experienced on drinking D_2O. Lewis[5] describes a mouse which had access to D_2O only and "the more he drank of the heavy water the thirstier he became." "The symptoms of distress that he showed seemed more pronounced after each dose, but not cumulative with succeeding doses." Since D_2O violently dehydrates living cells it is quite understandable that D_2O causes thirst and other osmotic effects.

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DISULFIDE FROM AMMONIUM SULFATE IN THE PRESENCE OF MASHED ROOT-TIPS OF PHASEOLUS VULGARIS

A NATURAL result of the finding of nearly ten years ago that the sulphydryl group and its partially oxi-

[4] D_2O was procured from the Stuart Oxygen Company. Its density was 1.1079 at 25°, and it was 99.9%+ pure.

[5] G. N. Lewis, SCIENCE, 79: 151–153, 1934.

dized derivatives play a significant part in the regulation of cell increase in number[1] has been stimulation of interest in the origin of the parent effective group.

The transformation of lifeless into living—the coming into expression in the chemical elements of those properties and combinations through which living substance is characterized is the becoming of growth.

Although there is an increasing literature dealing with the reactions of the biologically important sulfur groups *in vivo* and *in vitro*, and although there is much written of the ability of animals as well as plants to reduce the H_2S and even other sulfur compounds, not only elemental sulfur but also its highly oxidized derivatives such as sulfuric acid,[2, 3, 4] the beginning formation of the growth significant groups has yet to be traced.

Since soil is the source and plants the presumed medium for transformation of inorganic to organic—and since in root-tips there is concentration of SH and S.S. in organic form,[5] a first step in the search for the origin thereof would seem to be an inquiry into whether root-tips can make SH or S.S. from SO_4.

To do this the common bean (*Phaseolus vulgaris*) was sprouted on wet filter paper over absorbent cotton soaked in well-water in large Petri dishes. From the roots so obtained when 1 to 2 cm in length there was cut the distal 1.0 to 1.5 mm of meristematic tissue with a safety-razor blade. The tissue is recognizable by its yellowish tinge as distinct from the dead white of the proximal length. Some hundreds were cut and kept from drying for each trial. These were mashed and ground with a glass rod in the bottom of a 10 cc test-tube with a pinch of fine beach sand previously treated with cleaning solution and vigorously washed with well-water for 50 shakings. The mash was mixed with 1 cc well-water and centrifuged. Two to four drops of the supernatant fluid were added to each of two 10 cc test-tubes, the one containing 1 cc of a 0.1 per cent. $(NH_4)_2SO_4$ solution and the other plain well-water for control. Other controls were set up of sulfate solution and well-water alone; *viz.*, with no extract, usually two sets of each. After 18 to 24 hours the mixtures saturated with solid $(NH_4)_2SO_4$ were tested on the spot-plate for SH and S.S. with ammoniacal sodium nitroprusside.

Free SH was never found in these experiments which were repeated many times. The disulfide—or S.S. form—however, was detected more often than not after cyanide reduction in the extract-sulfate mixture. It was never found in the sulfate solution alone or well-water alone—and only infrequently in the extract-well-water mixture and then in very much less concentration than in the corresponding extract-sulfate mixture. A positive reaction was never obtained when the extract-sulfate mixture was boiled before incubation. This indicates that boiling destroyed some agent responsible for the reduction of SO_4 to S.S. The reaction was not inhibited in the unboiled extract-sulfate mixture on incubation in the presence of thymol.

These results suggest the presence of an enzyme in the root-tips of *Phaseolus vulgaris* which is capable of reducing SO_4 to S.S.

Although the possibility that the reduction derived from bacterial action is not completely eliminated, yet the fact that thymol did not inhibit its expression and the fact that a negative test was repeatedly given in the boiled extract-sulfate mixture despite opportunity for contamination, is evidence consistent with the enzyme postulate. At any rate the findings justify extension of the inquiry which will now be along more quantitative and other lines of obvious interest.

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[1] F. S. Hammett, *Proc. Am. Philos. Soc.*, 68: 151–161, 1929.

[2] L. Rubentschik, *Centralbl. Bakt.*, 11: Abt. 73, 483–496, 1928.

[3] A. Rippel and G. Behr, *Archiv. Mikrobiol.*, 7: 584–589, 1936.

[4] B. E. Kline, E. B. Hart, J. G. Halpin and C. E. Holmes, *Wis. Agr. Expt. Sta. Bull.*, 430 (Ann. Rept., 1933–1934).

[5] F. S. Hammett, *Protoplasma*, 5: 547–562, 1929.

EXACT PROBABILITIES IN CERTAIN CARD-MATCHING PROBLEMS

WE consider three cases:

THE 3 × 3 CASE

With a deck of nine cards composed of 3 suits of 3 cards each, the number of possible "runs" is known to be 1,680. If each of these possible runs is "matched" against any fixed run (taken from a duplicate deck), the number of "hits" found may be called the "score" for that run. I have computed by direct elementary means the exact frequency with which each possible score will occur in a complete cycle of runs. This result is given in Table A:

TABLE A

Score	Freq.	Rel. freq.
0	56	.03333
1	216	.12857
2	378	.22500
3	435	.25893
4	324	.19286
5	189	.11250
6	54	.03214
7	27	.01607
8	0	.0
9	1	.00060
	1,680	1.00000

The mean of the distribution is 3, and the standard deviation is 1.5.

THE 4×4 CASE

With a deck of sixteen cards composed of 4 suits of 4 cards each, the number of possible runs is known to be 63,063,000. The corresponding frequency table (computed by the same direct elementary process) is given as Table B.

TABLE B

Score	Freq.	Rel. freq.
0	748,521	.011,869,42
1	3,662,976	.058,084,39
2	8,607,744	.136,494,36
3	12,880,512	.204,248,32
4	13,731,616	.217,744,41
5	11,042,688	.175,105,66
6	6,928,704	.109,869,56
7	3,458,432	.054,840,91
8	1,395,126	.022,122,73
9	453,888	.007,197,37
10	122,016	.001,934,83
11	25,344	.000,401,88
12	4,824	.000,076,50–
13	512	.000,008,12
14	96	.000,001,52
15	0	.0
16	1	.000,000,02
	63,063,000	1.000,000,00

The mean is 4, and the standard deviation is $\sqrt{(3.2)}$, or 1.788,854,38.

THE 5×5 CASE

The case of greatest current interest concerns a deck of twenty-five cards composed of 5 suits of 5 cards each. With such a deck the number of possible runs is 623,360,743,125,120. The labor involved in a direct computation of the exact frequencies in this case appears to be prohibitive. By the use of more advanced methods, however, a solution for the 5×5 case has been worked out by my colleague, Dr. T. E. Sterne, and is presented in the following note.

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THE SOLUTION OF A PROBLEM IN PROBABILITY

IF a deck of 25 playing-cards, composed of 5 suits of 5 cards each, is shuffled at random and then compared with any fixed sequence of a similar deck, then the number, r, of coincidences of suit can take any value, with the exception of 24, from 0 to 25 inclusive. The theoretical probability of r, which I call $p(r)$, is a quantity of some current interest. The simple Binomial Law is not strictly applicable, since the coincidences are not independent.

By considering the probabilities in a 5×5 contingency table, I have computed the exact values of $p(r)$ for a few large values of r. They are:

r	$p(r)25!/(5!)^5$
21	44125
22	2500
23	250
24	0
25	1

I see no way to extend the exact computations practically to much smaller values of r. It is possible, however, to compute the moments of the distribution $p(r)$ exactly. The mean of r I find to be 5, and the second, third and fourth moments about the mean to be 25/6, 125/46 and 3625/69, respectively. All these values are exact. The distribution is thus of Pearson's Type I, and I have fitted a Type I curve to the above mean and moments with the results given in the second column of Table 1.

TABLE 1

r	$p(r)$	Binomial
0	.0043	.0038
1	.0247	.0236
2	.0730	.0708
3	.1374	.1358
4	.1852	.1867
5	.1919	.1960
6	1597	.1634
7	.1096	.1108
8	.0633	.0624
9	.0311	.0294
10	.0131	.0118
11	.0047	.0040
12	.0014	.0012
13	.0004	.0003
14	.0001	.0001
15	.0000	.0000
..	....	....
25	.0000	.0000

The values given by the Binomial Law appear in the third column, and appear to be fairly good approximations to the true values. The Binomial Law has the correct mean, but its second, third and fourth moments, 4, 2.4 and 48.16, are all somewhat too small. The Binomial Law would be exact were the coincidences of suit independent.

The values given in the second column above are expected to be correct to within a few units in the last place. Pearson Type I curves were fitted to the moments of the distributions of r in the 3×3 and 4×4 cases, and then compared with the exact values $p(r)$ computed for those cases by Professor Huntington. The accuracy of the Pearson curve in the 4×4 case was much greater than in the 3×3 case, and is shown in the comparison given in Table 2.

TABLE 2

r	True $p(r)$	Type I $p(r)$
0	.0119	.0112
1	.0581	.0570
2	.1365	.1374
3	.2042	.2059
4	.2177	.2176
5	.1751	.1741
6	.1099	.1095
7	.0548	.0552
8	.0221	.0224
9	.0072	.0073
10	.0019	.0019
11	.0004	.0004
12	.0001	.0001
13	.0000	.0000
..	....	....
16	.0000	.0000

Since the accuracy of the Type I approximation increases rapidly with the size of the deck, the values given in the second column for the 5×5 case are expected to be correct to within a very few units in the last place. Even in the 4×4 case, the accuracy of the Pearson Type I approximation is already so great that some 170,000 trials (a trial being an observation of r) would be required before one could distinguish with moderate certainty, from the observations, between the set of true probabilities and the direct Pearson approximation. To distinguish observationally between the true values and the binomial values, in the 5×5 case, would require some 30,000 trials.

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SCIENTIFIC APPARATUS AND LABORATORY METHODS

THE MEASUREMENT OF TURBIDITY IN COLORED MEDIA

THE measurement of turbidity photometrically is based on the assumption that there is a linear relationship between the amount of suspended matter and the intensity of the Tyndall beam. Although this holds moderately well within narrow limits when the sample is colorless and faintly turbid, the relationship between the amount of turbidity and the Tyndall beam intensity is much more complex at higher concentrations of suspended material as well as when coloring matter is present in solution.

One of the most disturbing factors is the concomitant weakening of the intensity of the Tyndall beam by absorption. When the suspending liquid is also colored, the absorption effect may be so great that it overbalances the scattering to an extent such that increasing turbidity may give a lower intensity of the Tyndall beam.

According to Sauer,[1] under these conditions the absolute turbidity is given by the following equation:

$$\text{Absolute Turbidity} = A \times f(k) \times D \times t \qquad (1)$$

where

A = Relative intensity of the Tyndall beam as measured with the Pulfrich photometer.

D = A factor varying with the thickness of the absorption cell.

t = The absolute turbidity of the glass standard of the instrument.

If d = Depth of layer of solution in centimeters, and k the coefficient of extinction

then
$$f(k) = \frac{kd(\sqrt{2}-1)\log_e 10}{10^{-kd}\{1-10^{-kd(\sqrt{2}-1)}\}} \qquad (1a)$$

In previous work the writers[2,3,4] have shown that the two empirical equations:

$$-\log T = C + N \qquad (2)$$

$$N = \frac{R\,b^C}{a} \qquad (3)$$

[1] Sauer, *Zeits. techn. Phys.*, 12: 149, 1931. See also Landt and Witte: *Zeits. Ver. deut. Zuckerind.*, 84: 462, 1934.

[2] Zerban, Sattler and Lorge, *Ind. Eng. Chem. Anal. Ed.*, 6: 178, 1934.

[3] Zerban, Sattler and Lorge, *Ibid.*, 7: 157, 1935.

hold for turbidity and color determinations for commercial raw cane sugar solutions as well as for white sugars.

C = Coloring matter expressed as $-\log T$.

N = Turbidity expressed as $-\log T$.

R = Intensity of the Tyndall beam = 100 A of Sauer.

T = Per cent. transmittancy.

$(-\log T) = 2 - \log T$.

a and b are constants.

We know now that the term b^C in equation (3) is equal to f(k), and that Sauer's equation is valid if C is substituted in place of the kd term in (1a). Hence the turbidity of a colored solution can be calculated either in terms of the absolute turbidity of Sauer, or else in the system used by the writers. Naturally the two methods are interrelated.

The final relationships are given by the following equations:

$$C = -\log T - \frac{R\,f(k)}{a} \qquad (4)$$

$$f(k) = \frac{\left[-\log T - \left(\frac{Rf(k)}{a}\right)\right](\sqrt{2}-1)\ \log_e 10}{10^{-\left(-\log T - \left(\frac{Rf(k)}{a}\right)\right)}\left\{1 - 10^{-\left[-\log T - \left(\frac{Rf(k)}{a}\right)\right](\sqrt{2}-1)}\right\}} \qquad (5)$$

When C is zero, f(k) is equal to 1.

Equation (5) is solved for varying values of C, which is the $-\log T - \frac{R\,f(k)}{a}$ term, and a table of corresponding f(k) values is thus obtained. Substitution of these C and f(k) values and increments of R into equation (4) yields a chart from which C is readily found from the $-\log T$ and the R values. Practically, C is found from curves based on the chart. The application to cane sugar solutions will be published elsewhere in the near future.

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[4] Zerban and Sattler, *Ibid.*, 9: 229, 1937.

AN ASBESTOS KCL BRIDGE AND A SIMPLE CALOMEL ELECTRODE

THE potentiometric determination of the O/R potential and pH at different depths in anaerobic oval tubes[1] measuring 360 mm in length and only 6×14 mm in cross section required the use of a small bore KCl bridge to form a junction between the medium and the calomel half cell. The liquid KCl bridge, the agar bridge and the ground glass sleeve commonly used for such measurements are impracticable for this purpose. Therefore an asbestos KCl bridge has been improvised which has proved to be entirely satisfactory, is easy to prepare and sufficiently sturdy to withstand sterilization. Visiting physicists and chemists who have seen this apparatus have suggested a multiplicity of applications for the asbestos KCl bridge so it is described in hopes of helping others, and without any claim for originality in the simplicity of the design.

Small threads of asbestos are freed of mineral impurities by bleaching in dilute HCl and water. Then each thread is heated to incandescence in a gas flame, after which it is sealed through the end of a glass tube of the desired length and diameter. The tubes can be filled with the KCl solution either with a long capillary pipette or by immersing in a vessel containing the hot solution and permitting it to cool.

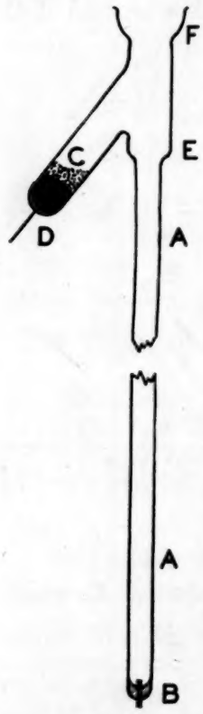

FIG. 1

We have prepared asbestos KCl bridges 400 mm long and only 0.2 mm in diameter, although in most of our work tubes 1.0 to 3.0 mm in diameter have been used. The asbestos thread provides for a slow leak of the KCl solution, thereby insuring a perfect ionic contact. The rate of leakage is controlled by the size of the asbestos fiber used. Satisfactory results have been obtained with tiny threads through which less than 0.01 cc of KCl solution leaks per hour.

The use of the asbestos KCl bridge was further expedited by connecting it directly to a calomel electrode, the design of which is illustrated by Fig. 1. It can be constructed in several ways, depending upon the desired dimensions of the apparatus and one's skill as a glass-blower. If the diameter of the tube AAB exceeds 3 mm, it is a matter of ease to seal on the short side-arm CD which serves as a receptacle for the mercury and calomel. A platinum wire sealed through the bottom of the side-arm tube CD provides for an electrical connection to the potentiometer. The top of the tube AAB may be flared at E to facilitate the introduction of the KCl solution with which the apparatus is filled after the asbestos fiber has been sealed through the bottom of the tube at B. The mercury and calomel paste are placed in the side-arm CD by means of a capillary pipette.

In case it is desirable to have the tube AAB smaller than 3 mm in diameter, it has been found simpler to construct the apparatus by sealing the tube to a short length of a larger tube EF, to which the side-arm CD is connected as illustrated. However, it is possible for any amateur laboratory technician to construct the entire apparatus from a fifteen-cent Y-tube in fifteen minutes. A platinum wire is sealed in one fork of the Y-tube and will serve as the receptacle for the mercury and calomel. The other fork is pulled out in a flame to give the desired length and diameter, after which an asbestos fiber is sealed through the end. The other end of the Y-tube is flared to facilitate the introduction of the solutions and the apparatus is ready to use.

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[1] S. C. Rittenberg, D. Q. Anderson and C. E. ZoBell; *Proc. Soc. Exp. Biol. and Med.*, 35: 652, 1937.

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Erratum: In the article by H. L. Hodes, G. I. Lavin and L. T. Webster, entitled "Antirabic immunization with culture virus rendered avirulent by ultra-violet light," printed in the issue of SCIENCE for November 12, 1937, the line "fatal dose of test virus, as contrasted with only one of" immediately before the table on the first column of page 448 was misplaced in the paging. It should be transferred to make it the last line of the text in that column.